DOCKET NO.: ORT-1199
Application No.: 09/521,527
Office Action Dated: April 22, 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Didier Leturcq

Confirmation No.: 1068

Application No.: 09/521,527

Group Art Unit: 1644

Filing Date: March 8, 2000

Examiner: Gerald R. Ewoldt

For: METHOD OF ISOLATING CD8+ CELLS, AND RELATED HYBRIDOMA CELLS, ANTIBODIES AND POLYPEPTIDES

DATE OF DEPOSIT: July 22, 2003

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID, ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

Myra McCormack

TYPED NAME: Myra H. McCormack
REGISTRATION NO.: 36,602

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY PURSUANT TO 37 CFR § 1.111

In response to the Official Action dated **April 22, 2003**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☒ **Remarks/Arguments** begin on page 5 of this paper.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Presently Amended) A method of isolating human CD8+ cells which comprises the steps of:

(a) contacting a sample of isolated peripheral mononuclear blood cells with a first antibody which specifically binds to ~~the sequence~~ an epitope comprising AAEGLDTQRFSG (SEQ ID NO:1) ~~or portion thereof~~, on CD8 molecules present on the surface of human CD8+ cells but does not activate the CD8+ cells once bound thereto, under conditions permitting the formation of a first complex between CD8+ cell and first antibody;

(b) separating from the sample any first antibody not present in the ~~resulting~~ first complex;

(c) contacting the sample with ~~a second,~~ an immobilized second antibody which specifically binds to the first antibody in the first complex, under conditions permitting the formation of an immobilized second complex between the first complex and the second antibody, thereby immobilizing the CD8+ cells present in the sample;

(d) separating ~~from~~ the ~~resulting~~ immobilized second complex from ~~the cells present in~~ the sample ~~which were not immobilized in step (c)~~;

(e) contacting the immobilized second complex ~~under suitable conditions~~ with an agent, which under suitable conditions causes ~~the~~ dissociation of the second complex into CD8+ cells and an immobilized third complex between the first antibody and second antibody; and

(f) separating the immobilized third complex from the CD8+ cells, thereby isolating the CD8+ cells.

2. (Canceled)

3. (Original) The method of claim 1, wherein the first antibody is a monoclonal antibody.

4. (Original) The method of claim 3, wherein the monoclonal antibody is produced by a hybridoma cell line selected from the group consisting of the cell line designated 37B1 (ATCC Accession No. HB-12441) and the cell line designated 8G6 (ATCC Accession No. HB-12657).

5. (Original) The method of claim 1, wherein the immobilized second antibody comprises an antibody operably affixed to a magnetic bead.

6. (Presently Amended) The method of claim 1, wherein the agent which causes the dissociation of immobilized third complex is the polypeptide designated CD8-3 ~~and~~ having the amino acid sequence AAEGLDTQRFSG (SEQ ID NO:1).

7. Canceled

8. Withdrawn

9. Canceled

10-12 Withdrawn

13. Canceled

14-16 Withdrawn

REMARKS/ARGUMENTS

I. Status of the Prosecution

Claims 1-6, 8, 10-12, and 14-16 are pending in the application. Claims 8, 10-12, and 14-16 are withdrawn as being drawn to nonelected inventions leaving claims 1-6 presently under consideration. Applicant's amendments of 7/13/01, 2/12/02 and 6/17/02 have been previously entered. Claims 1 and 6 have been amended, and claim 2 has been canceled herein.

II. The Trademark ATCC is Used Properly Throughout the Specification

The specification was objected to for allegedly containing an informality relating to the use of trademarks. In particular, the Office Action alleges that the use of the trademark "ATCC" should be capitalized and accompanied by the TM symbol in all instances where it appears and be accompanied by generic terminology. The Office Action further states that although the use of trademarks in patent applications is permissible, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicant respectfully traverses this requirement.

Guidance for the use of trademarks and names used in trade in patent applications is found at MPEP 608.01(v). In particular, the MPEP states that

> "if the product to which the trademark refers is set forth in such language that its identity is clear, the examiners are authorized to permit the use of the trademark if it is distinguished from common descriptive nouns ***by capitalization***. If the trademark has a fixed and definite meaning, it contains sufficient identification unless some physical or chemical characteristic of the article or material is involved in the invention."
>
> MPEP 608.01(v) (emphasis added).

The MPEP further provides that "[T]rademarks should be identified ***by capitalizing*** *each letter of the mark (in the case of word or letter marks)* ***or otherwise indicating*** the description of the mark (in the case of marks in the form of a symbol or device or other nontextual form)." (emphasis added)

It is clear from the MPEP that the use of capitalization is provided as an alternative to the use of a trademark symbol. Applicant respectfully submits that they have properly capitalized the trademark "ATCC" in each occurrence within the specification, and have thus respected the trademark and not used it in any manner which would adversely affect the validity of the mark. Additionally, the use of generic terminology to

clarify or augment the use of the mark is meaningless where as here, the allegedly offending trademark usage is simply an organization's acronym, which is widely recognized as such by the skilled artisan, is of fixed and definite meaning, and is not subject to arbitrary changes by the manufacturer and is not reflective of a product whose physical or chemical composition may vary. Nor is the usage of "ATCC" likely to be confused with the generic descriptions "depository" or "International Depository Authority." Applicant respectfully submits that proper care has been used to ensure proper usage of the trademark by placing it in capitals. There is no statutory or regulatory basis for the requirement made with the objection for both capitalization ***and*** a trademark symbol; and the MPEP provides for capitalization *or* the use of a description of a mark in the alternative. Similarly, Appendix I of the MPEP states that "[p]roper usage of trademarks requires that they be capitalized at all times." Here, Applicant has complied with the requirements, and submits nothing more is required. In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection.

III. The Claimed Methods Are Definite

A. The Claimed Methods Are Definite With Respect to the Use of the Trademark "ATCC"

Claim 4 stands rejected as allegedly indefinite for the recitation of the trademark "ATCC". The Office Action alleges that under *Ex parte Simpson* (218 USPQ 1020 (Bd. App. 1982), a claim where a trademark or trade name is used as a claim limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. § 112, second paragraph. The Office Action alleges that the claim scope cannot be certain since the trademark or trade name cannot be used properly to identify any particular material or product. The Office Action further alleges that a trademark or trade name does not identify a source of goods associated with the trademark or trade name. Applicant respectfully traverses the rejection.

Claim 4 is directed to a method of isolating human CD8+ cells comprising the steps of contacting the sample with a first antibody under conditions permitting the formation of a first complex between CD8+ cell and first antibody; separating from

the sample any first antibody not present in the first complex; contacting the sample with an immobilized second antibody under conditions permitting formation of an immobilized second complex; separating the immobilized second complex; contacting the immobilized second complex with an agent which under suitable conditions causes dissociation of the immobilized second complex into CD8+ cells and an immobilized third complex between the first antibody and the second antibody; and separating the immobilized third complex from the CD8+ cells thereby isolating the CD8+ cells; wherein the first antibody is a monoclonal antibody produced by a cell line selected from the group consisting of the cell line designated 37B1 (ATCC Accession No. HB-12441) and the cell line designated 8G6 (ATCC Accession No. HB-12657).

Applicants respectfully submit that the use of the trademark, ATCC, in this case, is not inapposite to the determination by the Board in *Simpson*. There, the Board determined that Simpson's use of a trademark (HYPALON) membrane was indefinite as a description given the scope of the claims. The Board, in approving a rejection under 35 U.S.C. § 112, second paragraph, stated that the purpose of that section is:

> "[t]o provide those who would endeavor, in future enterprise, to approach the area circumscribed by the claims of a patent, with the adequate notice demanded by due process of law, so that they may more readily and accurately determine the boundaries of protection involved and evaluate the possibility of infringement and dominance."

Simpson, 218 U.S.P.Q. at 1021 (citing *In re Hammack*, 427 F.2d 1378 (CCPA 1970)).

The *Simpson* Board went on to further consider that "[t]o determine whether the claim language is definite we must examine the claims to see whether the metes and bounds of the present invention can be adequately determined from the claim language." *Simpson*, 218 U.S.P.Q. 1021 (CCPA 1982) (quoting *In re Goffe*, 526 F.2d 1393 (CCPA 1975)). Although the Board concluded that the claims in *Simpson* were indefinite because they could be interpreted on the one hand to include only a narrow group of compounds actually employed by the owner of the HYPHALON trademark to produce the desired properties, or on the other hand, to encompass every synthetic resin. Because this ambiguity failed to satisfy the requirements of 35 U.S.C. § 112, second paragraph to notify the public of what they are not free to use, the Board concluded that "the use of a trademark *in the*

manner employed by appellant has resulted in claims which fail to meet this obligation. . ." *Id.* at 1022.

Unlike in *Simpson*, the use of the trademark "ATCC" in the instant application does not provide a source of ambiguity, but rather removes all possibility of ambiguity from the claim scope. The public is clearly put on notice as to what cell lines specifically are encompassed by the Applicant's claimed invention. The ATCC is a recognized IDA under the Budapest Treaty, and in addition, the proper identifying information is clearly provided in the specification and in the MPEP (see section 2405). The requirements of 35 U.S.C. § 112, second paragraph are completely satisfied with a precise reference to the cell lines used to produce the antibodies used in the claimed method. Applicant respectfully submits that nothing more is required under 35 U.S.C. § 112, second paragraph, nor could it be, given the detailed specificity with which the claimed invention is described. The citation to the deposited cell lines clarifies the claimed method. The skilled artisan is given an exacting description to the claimed biological material - the metes and bounds of the claimed method and the cell lines are perfectly delineated by the reference to the deposit. The Board's decision in *Simpson* can in no way be construed to

completely foreclose the use of trademarks in claims, but only in the vague and confusing manner used in that case. Applicant respectfully asserts that the use of the trademark in the instant claim is completely in keeping with the determination by the *Simpson* Board and is consistent with the requirements of 35 U.S.C. § 112, second paragraph. Unlike in *Simpson*, here, the skilled artisan immediately understands what is being claimed, and public is placed on clear notice as to precisely what they are not free to use. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Claim 6 stands rejected under 35 U.S.C. § 112, second paragraph as allegedly grammatically incorrect. Claim 6, as amended, does not recite the objected-to "and," thus rendering the grounds of the rejection moot. Applicant respectfully request withdrawal of the rejection.

IV. **The Specification Enables the Claimed Invention**

Claims 1-6 stand rejected under 35 U.S.C. § 112, first paragraph because while the Office Action acknowledges the specification is enabling for a method of isolating human CD8+ cells comprising the formation of a first complex between the

whole antibodies produced by the hybridomas designated by ATCC Accession Nos. HB-12441 or HB-12657 and SEQ ID NO:1, it allegedly does not provide reasonable enablement for a method of isolating human CD8+ cells comprising the formation of a first complex between the antibodies which bind SEQ ID NO:1 or portions thereof. Applicants respectfully traverse the rejection, in part.

The Office Action alleges the specification provides no guidance regarding which "portions" of SEQ ID NO:1 can be bound by an antibody, and which cannot. Applicants have amended the claims to remove the language "or portion thereof" with reference to SEQ ID NO:1, thus, the rejection with respect to a "portion" is rendered moot. Applicants respectfully request withdrawal of the rejection with respect to this language.

The Office Action also alleges that regarding "antibodies", the specification defines the term as encompassing "fragments thereof" at page 7, line 20. The Office Action further alleges that "fragments thereof" would comprise any and all possible fragments including single amino acids. As the Office Action states, it is well-known in the art that very short peptide fragments or single amino acids would not likely bind other peptide sequences.

When construing claims during patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification. *MPEP 2111. In re Hyatt*, 211 F.3d 1367, 1372 (Fed. Cir. 2000). The United States Patent and Trademark Office need not interpret claims as a court would do during an infringement suit, but rather,

> "the PTO is required to apply the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions. . .that may be afforded by the written description contained in applicant's specification."
> *MPEP 2111.*

Here, the interpretation of antibody is deemed to include any and all possible fragments including single amino acids. Applicants respectfully assert that this is improper for at least two reasons: (a) it is not reasonable under the standard provided in MPEP 2111; and (b) the claim limitation is taken out of context of the claim.

A. The Interpretation is Not Reasonable Under the MPEP-Required Standard

The MPEP clearly states that the broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *MPEP 2111*. Here, a skilled artisan would never conclude that the claim includes single amino acids or such small peptides that could not likely bind other peptide sequences. Those of skill in the art are very familiar with antibody fragments and no reasonable skilled artisan would consider the claim scope to include such nonfunctional fragments as are possible in a hypothetical, hypertechnical interpretation, but not reasonable. Further, it is not reasonable to take the definition out of context, the specification at page 7, lines 16-20 state that "[s]pecifically, the term 'antibody' includes polyclonal and monoclonal antibodies, and ***binding*** fragments thereof. Furthermore, the term 'antibody' includes chimeric antibodies and wholly synthetic antibodies and fragments thereof." The skilled artisan would reasonably conclude that the second usage of the term "fragments" is simply shorthand for binding fragments. The skilled artisan would not reasonably conclude

that suddenly the applicant is referring to nonbinding fragments or single amino acids. Applicant thus submits that the broadest, reasonable interpretation of the term "antibody" as used in the claims is in keeping with the definitions set out in the specification as a whole - particularly page 7, lines 14-29, and not an out-of-context emphasis on the single occurrence of the isolated term "fragment" on page 7, line 20.

B. The Claim Limitation is Taken Out of Context of the Claim.

The claim limitation at issue is not "a first antibody" but rather "a first antibody which specifically binds to an epitope. . . SEQ ID NO:1" The specification, on page 7, lines 23-27, defines "an antibody which 'specifically' binds to a stated epitope binds to that epitope with a dissociation constant of at least about 10-fold less than the dissociation constant with which it binds to any other epitope." When considering the claim limitation as a whole limitation, and not as isolated unmodified terms, it is clear that a skilled artisan could only conclude that what is claimed is limited to antibodies (and (binding) fragments thereof) which are capable of specifically binding to the SEQ ID NO:1. Thus, again, Applicant respectfully

submits that the only reasonable interpretation which a skilled artisan would consider is one in which the antibody must be capable of binding the SEQ ID NO:1 epitope - thus nonbinding fragments and single amino acids are precluded on the face of the claim and would not be considered by the skilled artisan. Binding fragments of antibodies are well-known in the art and the skilled artisan would understand from the claim language and the specification the identity of such binding fragments.

Based on the requirement for the broadest *reasonable* interpretation, and viewing the claim limitation as a whole in view of the definitions provided, Applicant submits that the specification enables one of skill to practice the invention as presently claimed without undue experimentation as to the antibody or its binding. Accordingly, Applicant respectfully requests reconsideration of the rejection under 35 U.S.C. § 112, first paragraph and withdrawal of the same.

V. The Written Description Satisfies the Requirements of 35 U.S.C. § 112, first paragraph

Claims 1-6 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably

convey to one of skill in the art that the inventor, at the time of filing was in possession of the claimed invention. Applicants traverse this rejection in part.

The claims are directed to a method of isolating human CD8+ cells comprising the steps of contacting the sample with a first antibody under conditions permitting the formation of a first complex between CD8+ cells and first antibody; separating from the sample any first antibody not present in the first complex; contacting the sample with an immobilized second antibody under conditions permitting formation of an immobilized second complex; separating the immobilized second complex; contacting the immobilized second complex with an agent, which under suitable conditions causes dissociation of the immobilized second complex into CD8+ cells and an immobilized third complex between the first antibody and the second antibody; and separating the immobilized third complex from the CD8+ cells thereby isolating the CD8+ cells.

The Office Action alleges that there is insufficient written description to show that Applicant was in possession of the "portion" of SEQ ID NO:1 bound by said first antibody. As addressed above, Applicant has amended the claim to remove this language, thus obviating the grounds of the rejection.

Accordingly, Applicant respectfully requests withdrawal of the rejection with respect to this language.

The Office Action further alleges that with respect to a "first antibody," there is insufficient written description to show that Applicant was in possession of any antibody other than those produced by the hybridomas designated ATCC Accession Nos HB-12441 and HB 12657, as recited in the claims. The Office Action reiterates the interpretation of the term antibody as discussed above to include fragments that bind SEQ ID NO:1 and alleges that no such fragments are disclosed, and that because the term would encompass an essentially unlimited genus, one of skill in the art would conclude that the specification fails to adequately describe the required antibody. Applicants respectfully traverse the rejection. "Generally, there is a inverse correlation between the level of skill and knowledge in the art and the specificity of the disclosure necessary to satisfy the written description requirement." *MPEP 2163*. The art of antibody production is not a new or unpredictable art, but rather is well-known. Here, Applicant has described and deposited two monoclonal antibody producing cell-lines. Further, and equally importantly, Applicant has provided the full amino acid sequence of the antigenic epitope - the root of

the biological specificity. Under the standard required by *Vas Cath v. Mahurkar* (935 F.2d 1555, 1563-4 (Fed. Cir. 1991), relied on in the Office Action, the Applicant need only convey with reasonable clarity that he was in possession of the invention. The Applicant respectfully submits that they need not describe the entire genus of antibodies, and what is well known (such as the making of an antibody to a peptide epitope) is preferably left out of the specification. All that is required is a written description which reasonably relates to the scope of the claimed invention. Here, given the exact description of the antigen as well as the description and deposit of two independent cell lines producing separate monoclonal antibodies, the skilled artisan would conclude that the Applicant was in possession of any of a wide variety of antibody molecules, including different classes, and could readily produce them in a wide variety of protocols, in a wide variety of organisms. Likewise the skilled artisan himself could do so by simply applying basic immunological techniques from any basic textbook or treatise. The skilled artisan must be understood to have this level of knowledge and skill at a bare minimum. To have made two different monoclonal antibodies is to have clearly possessed a great many other antibodies ("polyclonal") in the

process. Additionally, the production of binding fragments such as those defined in the specification is also well-known and basic in the art. A variety of binding fragments including those with one or multiple binding sites and containing various portions of the antibody molecule are known and readily made. The skilled artisan would conclude that inventor was in possession of these binding fragments as well. The important disclosure here, is not of the methods of making the antibodies, nor of their specific composition, but of the antigenic epitope which is used to generate the important biological specificity. Armed with the description of the antigen, the skilled artisan is able to envision the genus of claimed antibodies and would conclude that the Applicant was in possession of the entire genus on the filing date. Applicant respectfully submits that the description of the antigen, along with the monoclonal examples of first antibody provided are more than adequate to satisfy the requirements of 35 U.S.C. § 112, first paragraph with respect to the present invention. To require more here is to require the Applicant generally to reiterate what is well-known in the art - a practice the USPTO expressly has urged Applicants not to do. Applicant has both described the antibodies and enabled them to be made and used, and as such

deserves the *quid pro quo* of patent protection in exchange for this disclosure. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

VI. Conclusion

Applicants believe the present paper to be fully responsive to all outstanding issues. The current amendments are considered to place all the claims in condition for allowance and the same is earnestly sought in an early and favorable action. Should the examiner have any questions, he is invited to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Myra McCormack

Date: July 22, 2003

Myra H. McCormack
Registration No. 36,602

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6932